

What is claimed is:

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1. A compound comprising uricase covalently bonded via a linking group to polyethylene glycol, wherein the polyethylene glycol has a total weight average molecular weight of about 10,000 to about 30,000, and wherein the linking group is selected from the group consisting of a succinimide group, an amide group, an imide group, a carbamate group, an ester group, an epoxy group, a carboxyl group, a hydroxyl group, a carbohydrate, a tyrosine group, a cysteine group, a histidine group and combinations thereof.
  2. The compound of claim 1, wherein said linking group is a succinimide group.
  3. The compound of claim 2, wherein said succinimide group is succinimidyl succinate, succinimidyl propionate, succinimidyl carboxymethylate, succinimidyl succinamide, N-hydroxy succinimide or combinations thereof.
  4. The compound of claim 3, wherein said succinimide group is succinimidyl succinate, succinimidyl propionate or combinations thereof.
  5. The compound of claim 1, wherein said uricase is derived from a microorganism selected from the group consisting of *Aspergillus flavus*, *Candida utilis*, *Arthrobacter protoformiae*, and combinations thereof.
  6. The compound of claim 5, wherein said microorganism is *Aspergillus flavus*.
  7. The compound of claim 5, wherein said microorganism is *Candida utilis*.
  8. The compound of claim 5, wherein said microorganism is *Arthrobacter protoformiae*.
  9. The compound of claim 1 wherein the polyethylene glycol has an average molecular weight of about 20,000.
  10. The compound of claim 1 wherein said uricase is covalently bonded to about 10 to about 25 polyethylene glycol molecules.

11. The compound of claim 1, wherein said uricase is covalently bonded to about 18 to about 22 polyethylene glycol molecules.
12. The compound of claim 1, wherein said uricase is covalently bonded to about 20 polyethylene glycol molecules.
13. The compound of claim 1 wherein polyethylene glycol is covalently attached to uricase at residues other than Lys<sup>156</sup> of SEQ ID NO:6.
14. The compound of claim 1 wherein polyethylene glycol is covalently attached to uricase at residues other than Lys<sup>167</sup> of SEQ ID NO:6.
15. The compound of claim 1 wherein polyethylene glycol is covalently attached to uricase at residues other than Lys<sup>12</sup> of SEQ ID NO:6.
16. The compound of claim 1 wherein polyethylene glycol is covalently attached to uricase at residues other than Lys<sup>64</sup> of SEQ ID NO:6.
17. The compound of claim 1 wherein polyethylene glycol is covalently attached to uricase at residues other than Lys<sup>262</sup> of SEQ ID NO:6.
18. The compound of claim 1 wherein polyethylene glycol is covalently attached to uricase at residues other than Lys<sup>117</sup> of SEQ ID NO:6.
19. The compound of claim 1 wherein polyethylene glycol is covalently attached to uricase at residues other than Lys<sup>16</sup>, Lys<sup>28</sup>, and Lys<sup>72</sup> of SEQ ID NO:6.
20. The compound of claim 1 wherein polyethylene glycol is covalently attached to uricase at residues other than Lys<sup>12</sup>, Lys<sup>16</sup>, Lys<sup>28</sup>, Lys<sup>64</sup>, Lys<sup>72</sup>, Lys<sup>117</sup>, Lys<sup>156</sup>, Lys<sup>167</sup>, and Lys<sup>262</sup> of SEQ ID NO:6.
21. The compound of any one of claims 1 or 13-20 wherein polyethylene glycol is covalently attached to uricase at one or more lysine residues.
22. A method of enhancing the circulating half life of uricase comprising modifying said uricase by covalently bonding said uricase via a linking group to polyethylene glycol, wherein the polyethylene glycol has a total weight average molecular weight of

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cont.*

about 10,000 to about 30,000, and wherein the linking group is selected from the group consisting of a succinimide group, an amide group, an imide group, a carbamate group, an ester group, an epoxy group, a carboxyl group, a hydroxyl group, a carbohydrate, a tyrosine group, a cysteine group, a histidine group and combinations thereof.

23. The method of claim 22 wherein the polyethylene glycol has an average molecular weight of about 20,000.

24. The method of claim 22, wherein said uricase is covalently bonded to about 10 to about 25 polyethylene glycol molecules.

25. The method of claim 22, wherein said uricase is covalently bonded to about 18 to about 22 polyethylene glycol molecules.

26. A method of enhancing the anti-uric acid activity of uricase comprising modifying said uricase by covalently bonding said uricase via a linking group to polyethylene glycol, wherein the polyethylene glycol has a total weight average molecular weight of from about 10,000 to about 30,000, and wherein the linking group is selected from the group consisting of a succinimide group, an amide group, an imide group, a carbamate group, an ester group, an epoxy group, a carboxyl group, a hydroxyl group, a carbohydrate, a tyrosine group, a cysteine group, a histidine group and combinations thereof.

27. The method of claim 26 wherein the polyethylene glycol has an average molecular weight of about 20,000.

28. The method of claim 26, wherein said uricase is covalently bonded to about 10 to about 25 polyethylene glycol molecules.

29. The method of claim 26, wherein said uricase is covalently bonded to about 18 to about 22 polyethylene glycol molecules.

30. The method of claim 26 wherein said uricase is covalently bonded to about 20 polyethylene glycol molecules.

31. A method of reducing uric acid levels in a patient comprising administering to said patient a therapeutically effective amount of the compound of claim 1.

32. The method of claim 31, wherein said patient has hypouricemia.
33. The method of claim 31, wherein said polyethylene glycol has an average molecular weight of about 20,000
34. The method of claim 31, wherein said linking group is a succinimide group.
35. The method of claim 32, wherein said succinimide group is succinimidyl succinate, succinimidyl propionate, succinimidyl carboxymethylate, succinimidyl succinamide, N-hydroxy succinimide or combinations thereof.
36. A method of treating uric acid related disorders in a patient comprising administering to said patient a therapeutically effective amount of the compound of claim 1.
37. The method of claim 36, wherein said polyethylene glycol has an average molecular weight of about 20,000
38. The method of claim 36 wherein polyethylene glycol molecule is covalently attached to uricase at residues other than Lys<sup>12</sup>, Lys<sup>16</sup>, Lys<sup>28</sup>, Lys<sup>64</sup>, Lys<sup>72</sup>, Lys<sup>117</sup>, Lys<sup>156</sup>, Lys<sup>167</sup>, and Lys<sup>262</sup> of SEQ ID NO:6.
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39. A compound comprising uricase coupled to polyethylene glycol, wherein the polyethylene glycol has a total weight average molecular weight of about 10,000 to about 30,000.
40. The compound of claim 39 wherein the polyethylene glycol has an average molecular weight of about 20,000.
41. The compound of claim 39, wherein said uricase is covalently bonded to about 10 to about 25 polyethylene glycol molecules.
42. The compound of claim 39, wherein said uricase is covalently bonded to about 18 to about 22 polyethylene glycol molecules.

43. The compound of claim 39, wherein said uricase is coupled to about 20 polyethylene glycol molecules.

44. The compound of claim 39 wherein polyethylene glycol is coupled to uricase at residues other than Lys<sup>12</sup>, Lys<sup>16</sup>, Lys<sup>28</sup>, Lys<sup>64</sup>, Lys<sup>72</sup>, Lys<sup>117</sup>, Lys<sup>156</sup>, Lys<sup>167</sup>, and Lys<sup>262</sup> of SEQ ID NO:6.

45. A method of enhancing the anti-uric acid activity of uricase comprising modifying said uricase by covalently bonding said uricase to polyethylene glycol, wherein the polyethylene glycol has a total weight average molecular weight of from about 10,000 to about 30,000.

46. The method of claim 45, wherein said uricase is covalently bonded to about 20 polyethylene glycol molecules.

47. The method of claim 45 wherein the polyethylene glycol has an average molecular weight of about 20,000.

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